#36

Patent
Attorney's Docket No. 100084.402

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Oct. 20, 01

In the Patent Application of	)	
Bjorck *et al.*	)	Group Art Unit: 1645
Application No.: 08/325,278	)	Examiner: N. M. Minnifield
Filed: October, 26, 1994	)	
For: PROTEIN L AND HYBRID PROTEINS THEREOF	)	

DECLARATION OF ULF SJÖBRING PURSUANT TO 37 C.F.R. 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Considered 1-15-02 MN

Sir:

I, Ulf Sjöbring, hereby declare:

1) I am co-inventor on the above-referenced US Patent Application No. 08/325,278, entitled *Protein L and Hybrid Proteins Thereof* and co-author on the journal article entitled *Structure of Peptostreptococcal Protein L and Identification of a Repeated Immunoglobulin Light Chain Binding Domain.* (Kastern, *et al.*, J. Biol. Chem. 1992, 267 (18):12820-5).

2) There is no specific section in Kastern, *et al.*, *JBC*, 1992 pointing out the difficulties in obtaining the full sequence of protein L. However, the following issues relating to this article and previously published data supports the existence of such problems:

(i) A long period elapsed between the description of protein L (Björck, 1988, J. Immunol. or patent 1987) and the sequence of the protein L gene. The difficulties were due to problems with cloning and sequence determination.

(ii). The partial sequence described by Kastern, *et al.*, *Infection and Immunity*, 1990, derive from small inserts incapable of directing expression of a functional (*i.e.*, Ig-binding) protein L protein/peptide. This means that in Kastern, *et al.*, 1990, there is actually no formal evidence demonstrating that the sequenced inserts contained in the lambdaZAP vector clones were really identical to those present in protein L (this became obvious only in Kastern, *et al.*, 1992).

Specifically, as long as a link between the recombinant insert and the functional property (or its antigenicity) of the insert has not been established:

(a) it cannot be excluded that although the short peptide sequence obtained by trypsin cleavage of protein L was identical with what was later to be demonstrated to be the deduced amino acid sequence of protein L, these sequences could be derived from related proteins, not necessarily exhibiting the Ig-binding property of protein L. For example, there are a number of examples of closely linked genes that are structurally similar but that encode different functions, including different sequence divergence. The group A streptococcal Mrp, Emm and Enn proteins provide an example of such a phenomenon, where each of these proteins possess regions that are highly homologous or identical, but where the binding properties are different due to differences in other regions of the proteins.

(b) along a similar line of reasoning (*i.e.*, the lack of link between the identified sequences and the ability to bind Ig or at least to share common antigenic determinants) there exists the possibility that the amino acid sequences obtained from what was believed to be pure protein L could have actually been derived from a contaminant in the protein L preparation.

(iii). Cloning of larger fragments in the lambdaZAP system than the 220 base-pair long fragments described in Kastern *et al.*, 1990, proved unsuccessful. To enable cloning and sequence determination, a different system had to be used—ligating TaqI DNA fragments into the M13 system. This change of strategy is described

by Kastern *et al.*, *JBC*, 1992, in Materials and Methods in the section headed DNA Manipulations.

(iv). The reasons for the difficulties are partly obscure; it is however well-known that cloning and expression in *E. coli* of proteins with the hydrophobic membrane anchor domain that is present in protein L is difficult. As previously pointed out, the repetitive nature of the Ig-binding repeats of protein L made sequence determination difficult.

4) I declare that all statements made herein of my own knowledge are true and that all statements made on information are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date July 18 2007

Ulf Sjöbring

D:\NrPortbl\iManage\JULIEU\145720_1.DOC

#38

PATENT

I hereby certify that on the date specified below, this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to the Commissioner for Patents, Washington, DC 20231.

Oct. 2001

September 24, 2001
Date

Carol Williams

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Lars Björck and Ulf Sjöbring
Application No.	:	08/325,278
Filed	:	October 26, 1994
For	:	PROTEIN L AND HYBRID PROTEINS THEREOF

Examiner	:	Nita Minnifield
Art Unit	:	1645
Docket No.	:	100084.402
Date	:	September 24, 2001

Commissioner for Patents
Washington, DC 20231

DECLARATION OF WILLIAM KASTERN,
LARS BJÖRCK AND ULF SJÖBRING

Original Declaration as signed is attached.

PATENT

I herby certify that on the date specified below, this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, DC 20231.

Date David D. McMasters

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Lars Björck and Ulf Sjöbring
Application No.	:	08/325,278
Filed	:	October 26, 1994
For	:	PROTEIN L AND HYBRID PROTEINS THEREOF
	:	Examiner: Anthony C. Caputa, Ph.D.
		Art Unit : 1817
		Docket No. : 100084.402
		Date :

considered 1-15-02 MM

Assistant Commissioner for Patents
Washington, DC 20231

DECLARATION OF WILLIAM KASTERN, LARS BJÖRK AND ULF SJÖBRING

1. Lars Björck and Ulf Sjöbring are co-inventors, and have read, and understand the above-identified application.

2. We have read the Examiner's Office Action dated March 25, 1997 with respect to the above-identified application. Briefly, within that Offce action, the Examiner rejected claims 1 and 11-13 under 35 U.S.C.§ 102(a) as being anticipated

by Kastern, Sjöbring and Björck, (*J. Biol. Chemistry* 267(18):12820-25, (1992)).

3. We are co-authors, of the above-noted article published in the *Journal of Biological Chemistry*. In addition, we are familiar with the development of the subject matter described within this article.

4. Dr. Kastern was a participant in the very early stages of this research, mostly as a consultant who gave general advice about procedures and techniques. As such, he was made first author on the 1992 paper (Kastern *et al*, *J. Biol. Chem.* 267(18) 12820-12825 (1992)) as a matter of professional courtesy.

5. As a result of the participation of Dr. Kastern, the substance of the Kastern *et al* article was the work of only the above-named inventors.

6. We declare further that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

April 3, 1998
Date

William Kastern

March 19, 1998
Date

Lars Björck

March 19, -98
Date

Ulf Sjöbring

6300 Columbia Center
701 Fifth Avenue,
Seattle, Washington 98104-7092
(206) 622-4900
Fax: (206) 682-6031